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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,464	03/28/2001	Martin Friede	B45070-1 US1	1150
23347	7590	12/22/2008	EXAMINER	
GLAXOSMITHKLINE			LUCAS, ZACHARIAH	
CORPORATE INTELLECTUAL PROPERTY, MAI B482				
FIVE MOORE DR., PO BOX 13398			ART UNIT	PAPER NUMBER
RESEARCH TRIANGLE PARK, NC 27709-3398			1648	
			NOTIFICATION DATE	DELIVERY MODE
			12/22/2008	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Advisory Action Before the Filing of an Appeal Brief</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/819,464	FRIEDE ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Zachariah Lucas	1648

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 September 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1.  The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a)  The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.  
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2.  The Notice of Appeal was filed on 11 November 2008. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3.  The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
  - (a)  They raise new issues that would require further consideration and/or search (see NOTE below);
  - (b)  They raise the issue of new matter (see NOTE below);
  - (c)  They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d)  They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4.  The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5.  Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
6.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7.  For purposes of appeal, the proposed amendment(s): a)  will not be entered, or b)  will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 74-84, 94 and 95.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8.  The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9.  The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10.  The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11.  The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.
12.  Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_
13.  Other: \_\_\_\_\_.

/Zachariah Lucas/  
Primary Examiner, Art Unit 1648

Continuation of 11. does NOT place the application in condition for allowance because: Claims 74-76, 78, 80, 82-84, 94, and 96 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lipford (Vaccine 12: 72-80) in view of the teachings of Kensil (U.S. 5,583,112). Claims 77, 79, and 81 were rejected under 35 U.S.C. 103(a) as being unpatentable over either Lipford in view of Kensil, and further in view of Prieels et al. (WO 94/00153).

The Applicant traverses the rejections on the basis that the Examiner is maintaining the rejection on the grounds that the claimed ratio of saponin to sterol would be obvious by routine optimization. The Applicant argues that a ratio may only be obvious through routine optimization where the variable is a result-effective variable, and that the Examiner has not suggested any result that may be made through the optimization of the ratio of sterol to saponin. The argument is noted, but not found persuasive.

It is first noted that the assertion of routine optimization was made only with respect to the limitations of claim 95. See, page 4 of the action mailed on March 9, 2007. The argument is not found persuasive with respect to the remainder of the claims for the reasons indicated in the action mailed on page 3 of the action mailed on July 17, 2006.

With respect to claim 95, the argument is also not found persuasive. First, it is noted that the teachings of Kensil indicate that QS-21 has somewhat reduced hemolytic activity compared to Quil A. Figure 11. Second, Lipford indicates that the hemolytic activity of saponins appear to be due, at least in part, to its ability to intercalate with cholesterol containing membranes. Page 78, left column. From these teachings, it would be obvious to those of ordinary skill in the art that the presence of the cholesterol in ISCOMs may at least partially responsible for the reduced hemolytic activity of the saponin in the ISCOM formulation. Thus, in view of the teachings of Kensil indicating that the hemolytic properties of the Quil A fractions vary from those of Quil A itself, it would have been obvious to those of ordinary skill in the art to vary the amount of cholesterol in the ISCOMs to determine the optimal concentration of sterols required to minimize the hemolytic activity of the saponin. The Applicant's argument is therefore not found persuasive, and the rejection is maintained. .